



# SEQUENCE LISTING

<110> Gravel, Roy A,  
Rozen, Rima  
Leclerc, Daniel  
Wilson, Aaron  
Rosenblatt, David

<120> HUMAN METHIONINE SYNTHASE REDUCTASE:  
CLONING, AND METHODS FOR EVALUATING RISK OF NEURAL TUBE  
DEFECTS, CARDIOVASCULAR DISEASE, CANCER, AND DOWN'S SYNDROME

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<400> 24

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<210> 38  
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<210> 39  
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<213> Homo sapiens

<400> 42

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<210> 44  
<211> 698  
<212> PRT  
<213> Homo sapiens

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Glu Thr Ala Pro Leu Val Val Val Val Ser Thr Thr Gly Thr Gly Asp  
50 55 60  
Pro Pro Asp Thr Ala Arg Lys Phe Val Lys Glu Ile Gln Asn Gln Thr  
65 70 75 80  
Leu Pro Val Asp Phe Phe Ala His Leu Arg Tyr Gly Leu Leu Gly Leu  
85 90 95  
Gly Asp Ser Glu Tyr Thr Tyr Phe Cys Asn Gly Gly Lys Ile Ile Asp  
100 105 110  
Lys Arg Leu Gln Glu Leu Gly Ala Arg His Phe Tyr Asp Thr Gly His  
115 120 125  
Ala Asp Asp Cys Val Gly Leu Glu Leu Val Val Glu Pro Trp Ile Ala  
130 135 140  
Gly Leu Trp Pro Ala Leu Arg Lys His Phe Arg Ser Ser Arg Gly Gln  
145 150 155 160  
Glu Glu Ile Ser Gly Ala Leu Pro Val Ala Ser Pro Ala Ser Leu Arg  
165 170 175  
Thr Asp Leu Val Lys Ser Glu Leu Leu His Ile Glu Ser Gln Val Glu  
180 185 190  
Leu Leu Arg Phe Asp Asp Ser Gly Arg Lys Asp Ser Glu Val Leu Lys  
195 200 205  
Gln Asn Ala Val Asn Ser Asn Gln Ser Asn Val Val Ile Glu Asp Phe  
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Glu Ser Ser Leu Thr Arg Ser Val Pro Pro Leu Ser Gln Ala Ser Leu  
225 230 235 240  
Asn Ile Pro Gly Leu Pro Pro Glu Tyr Leu Gln Val His Leu Gln Glu  
245 250 255  
Ser Leu Gly Gln Glu Glu Ser Gln Val Ser Val Thr Ser Ala Asp Pro  
260 265 270  
Val Phe Gln Val Pro Ile Ser Lys Ala Val Gln Leu Thr Thr Asn Asp  
275 280 285  
Ala Ile Lys Thr Thr Leu Leu Val Glu Leu Asp Ile Ser Asn Thr Asp  
290 295 300  
Phe Ser Tyr Gln Pro Gly Asp Ala Phe Ser Val Ile Cys Pro Asn Ser  
305 310 315 320  
Asp Ser Glu Val Gln Ser Leu Leu Gln Arg Leu Gln Leu Glu Asp Lys  
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Arg Glu His Cys Val Leu Leu Lys Ile Lys Ala Asp Thr Lys Lys Lys  
340 345 350  
Gly Ala Thr Leu Pro Gln His Ile Pro Ala Gly Cys Ser Leu Gln Phe

355	Ile Phe Thr Trp Cys Leu Glu	360	Ile Arg Ala Ile Pro Lys Lys Ala Phe
370	Leu Arg Ala Leu Val Asp Tyr Thr Ser Asp Ser Ala Glu Lys Arg Arg	380	
385	Leu Gln Glu Leu Cys Ser Lys Gln Gly Ala Ala Asp Tyr Ser Arg Phe	395	400
405	Val Arg Asp Ala Cys Ala Cys Leu Leu Asp Leu Leu Leu Ala Phe Pro	410	415
420	Ser Cys Gln Pro Pro Leu Ser Leu Leu Leu Glu His Leu Pro Lys Leu	425	430
435	Gln Pro Arg Pro Tyr Ser Cys Ala Ser Ser Ser Leu Phe His Pro Gly	440	445
450	Lys Leu His Phe Val Phe Asn Ile Val Glu Phe Leu Ser Thr Ala Thr	455	460
465	Thr Glu Val Leu Arg Lys Gly Val Cys Thr Gly Trp Leu Ala Leu Leu	470	475
485	Val Ala Ser Val Leu Gln Pro Asn Ile His Ala Ser His Glu Asp Ser	490	495
500	Gly Lys Ala Leu Ala Pro Lys Ile Ser Ile Ser Pro Arg Thr Thr Asn	505	510
515	Ser Phe His Leu Pro Asp Asp Pro Ser Ile Pro Ile Ile Met Val Gly	520	525
530	Pro Gly Thr Gly Ile Ala Pro Phe Ile Gly Phe Leu Gln His Arg Glu	535	540
545	Lys Leu Gln Glu Gln His Pro Asp Gly Asn Phe Gly Ala Met Trp Leu	550	555
565	Phe Phe Gly Cys Arg His Lys Asp Arg Asp Tyr Leu Phe Arg Lys Glu	570	575
580	Leu Arg His Phe Leu Lys His Gly Ile Leu Thr His Leu Lys Val Ser	585	590
595	Phe Ser Arg Asp Ala Pro Val Gly Glu Glu Glu Ala Pro Ala Lys Tyr	600	605
610	Val Gln Asp Asn Ile Gln Leu His Gly Gln Gln Val Ala Arg Ile Leu	615	620
625	Leu Gln Glu Asn Gly His Ile Tyr Val Cys Gly Asp Ala Lys Asn Met	630	635
645	Ala Lys Asp Val His Asp Ala Leu Val Gln Ile Ile Ser Lys Glu Val	650	655
660	Gly Val Glu Lys Leu Glu Ala Met Lys Thr Leu Ala Thr Leu Lys Glu	665	670
675	Glu Lys Arg Tyr Leu Gln Asp Ile Trp Ser	680	685
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 <212> DNA  
 <213> Homo sapiens

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 ggcaccggag acccaccgga cacagccgcg aagtttggtta aggaaatata gaaccaaaca 240  
 ctgccgggtg atttcttttg tcacctgcgg tatgggttac tgggtctcgg tgattcagaa 300  
 tacacctact ttgcaatgg ggggaagata attgataaac gacttcaaga gcttgaggcc 360

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gatgcccttg tgcaaataat aagcaaagag gttggagttg aaaaactaga agcaatgaaa 2040
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<210> 46

<211> 697

<212> PRT

<213> Homo sapiens

<400> 46

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 20          25          30
Ala Asp Leu His Cys Ile Ser Glu Ser Asp Lys Tyr Asp Leu Lys Thr
 35          40          45
Glu Thr Ala Pro Leu Val Val Val Ser Thr Thr Gly Thr Gly Asp
 50          55          60
Pro Pro Asp Thr Ala Arg Lys Phe Val Lys Glu Ile Gln Asn Gln Thr
 65          70          75          80
Leu Pro Val Asp Phe Phe Ala His Leu Arg Tyr Gly Leu Leu Gly Leu
 85          90          95
Gly Asp Ser Glu Tyr Thr Tyr Phe Cys Asn Gly Gly Lys Ile Ile Asp
100         105         110
Lys Arg Leu Gln Glu Leu Gly Ala Arg His Phe Tyr Asp Thr Gly His
115         120         125
Ala Asp Asp Cys Val Gly Leu Glu Leu Val Val Glu Pro Trp Ile Ala
130         135         140
Gly Leu Trp Pro Ala Leu Arg Lys His Phe Arg Ser Ser Arg Gly Gln
145         150         155         160
Glu Glu Ile Ser Gly Ala Leu Pro Val Ala Ser Pro Ala Ser Leu Arg

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Glu	Ser	Ser	Leu	Thr	Arg	Ser	Val	Pro	Pro	Leu	Ser	Gln	Ala	Ser	Leu		
225					230					235					240		
Asn	Ile	Pro	Gly	Leu	Pro	Pro	Glu	Tyr	Leu	Gln	Val	His	Leu	Gln	Glu		
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Val	Phe	Gln	Val	Pro	Ile	Ser	Lys	Ala	Val	Gln	Leu	Thr	Thr	Asn	Asp		
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Ala	Ile	Lys	Thr	Thr	Leu	Leu	Val	Glu	Leu	Asp	Ile	Ser	Asn	Thr	Asp		
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Phe	Ser	Tyr	Gln	Pro	Gly	Asp	Ala	Phe	Ser	Val	Ile	Cys	Pro	Asn	Ser		
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Asp	Ser	Glu	Val	Gln	Ser	Leu	Leu	Gln	Arg	Leu	Gln	Leu	Glu	Asp	Lys		
				325					330					335			
Arg	Glu	His	Cys	Val	Leu	Leu	Lys	Ile	Lys	Ala	Asp	Thr	Lys	Lys	Lys		
			340					345					350				
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Ile	Phe	Thr	Trp	Cys	Leu	Glu	Ile	Arg	Ala	Ile	Pro	Lys	Lys	Ala	Phe		
	370					375					380						
Leu	Arg	Ala	Leu	Val	Asp	Tyr	Thr	Ser	Asp	Ser	Ala	Glu	Lys	Arg	Arg		
385					390					395					400		
Leu	Gln	Glu	Leu	Cys	Ser	Lys	Gln	Gly	Ala	Ala	Asp	Tyr	Ser	Arg	Phe		
				405					410					415			
Val	Arg	Asp	Ala	Cys	Ala	Cys	Leu	Leu	Asp	Leu	Leu	Leu	Ala	Phe	Pro		
			420					425					430				
Ser	Cys	Gln	Pro	Pro	Leu	Ser	Leu	Leu	Leu	Glu	His	Leu	Pro	Lys	Leu		
		435					440					445					
Gln	Pro	Arg	Pro	Tyr	Ser	Cys	Ala	Ser	Ser	Ser	Leu	Phe	His	Pro	Gly		
	450					455					460						
Lys	Leu	His	Phe	Val	Phe	Asn	Ile	Val	Glu	Phe	Leu	Ser	Thr	Ala	Thr		
465					470					475					480		
Thr	Glu	Val	Leu	Arg	Lys	Gly	Val	Cys	Thr	Gly	Trp	Leu	Ala	Leu	Leu		
				485					490					495			
Val	Ala	Ser	Val	Leu	Gln	Pro	Asn	Ile	His	Ala	Ser	His	Glu	Asp	Ser		
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Gln	Asp	Asn	Ile	Gln	Leu	His	Gly	Gln	Gln	Val	Ala	Arg	Ile	Leu	Leu
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Gln	Glu	Asn	Gly	His	Ile	Tyr	Val	Cys	Gly	Asp	Ala	Lys	Asn	Met	Ala
				645						650					655
Lys	Asp	Val	His	Asp	Ala	Leu	Val	Gln	Ile	Ile	Ser	Lys	Glu	Val	Gly
			660						665					670	
Val	Glu	Lys	Leu	Glu	Ala	Met	Lys	Thr	Leu	Ala	Thr	Leu	Lys	Glu	Glu
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 <212> DNA  
 <213> Homo sapiens

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<210> 48  
 <211> 689  
 <212> PRT

<213> Homo sapiens

<400> 48

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Asp	Leu	His	Cys	Ile	Ser	Glu	Ser	Asp	Lys	Tyr	Asp	Leu	Lys	Thr	Glu
	35					40					45				
Thr	Ala	Pro	Leu	Val	Val	Val	Val	Ser	Thr	Thr	Gly	Thr	Gly	Asp	Pro
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Pro	Asp	Thr	Ala	Arg	Lys	Phe	Val	Lys	Glu	Ile	Gln	Asn	Gln	Thr	Leu
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Pro	Val	Asp	Phe	Phe	Ala	His	Leu	Arg	Tyr	Gly	Leu	Leu	Gly	Leu	Gly
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Asp	Ser	Glu	Tyr	Thr	Tyr	Phe	Cys	Asn	Gly	Gly	Lys	Ile	Ile	Asp	Lys
	100							105				110			
Arg	Leu	Gln	Glu	Leu	Gly	Ala	Arg	His	Phe	Tyr	Asp	Thr	Gly	His	Ala
	115						120					125			
Asp	Asp	Cys	Val	Gly	Leu	Glu	Leu	Val	Val	Glu	Pro	Trp	Ile	Ala	Gly
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Leu	Trp	Pro	Ala	Leu	Arg	Lys	His	Phe	Arg	Ser	Ser	Arg	Gly	Gln	Glu
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Glu	Ile	Ser	Gly	Ala	Leu	Pro	Val	Ala	Ser	Pro	Ala	Ser	Leu	Arg	Thr
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Asp	Leu	Val	Lys	Ser	Glu	Leu	Leu	His	Ile	Glu	Ser	Gln	Val	Glu	Leu
	180							185					190		
Leu	Arg	Phe	Asp	Asp	Ser	Gly	Arg	Lys	Asp	Ser	Glu	Val	Leu	Lys	Gln
	195					200					205				
Asn	Ala	Val	Asn	Ser	Asn	Gln	Ser	Asn	Val	Val	Ile	Glu	Asp	Phe	Glu
	210					215					220				
Ser	Ser	Leu	Thr	Arg	Ser	Val	Pro	Pro	Leu	Ser	Gln	Ala	Ser	Leu	Asn
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Ile	Pro	Gly	Leu	Pro	Pro	Glu	Tyr	Leu	Gln	Val	His	Leu	Gln	Glu	Ser
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Leu	Gly	Gln	Glu	Glu	Ser	Gln	Val	Ser	Val	Thr	Ser	Ala	Asp	Pro	Val
		260				265						270			
Phe	Gln	Val	Pro	Ile	Ser	Lys	Ala	Val	Gln	Leu	Thr	Thr	Asn	Asp	Ala
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Ile	Lys	Thr	Thr	Leu	Leu	Val	Glu	Leu	Asp	Ile	Ser	Asn	Thr	Asp	Phe
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Ser	Tyr	Gln	Pro	Gly	Asp	Ala	Phe	Ser	Val	Ile	Cys	Pro	Asn	Ser	Asp
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Glu	His	Cys	Val	Leu	Leu	Lys	Ile	Lys	Ala	Asp	Thr	Lys	Lys	Lys	Gly
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Ala	Thr	Leu	Pro	Gln	His	Ile	Pro	Ala	Gly	Cys	Ser	Leu	Gln	Phe	Ile
	355					360						365			
Phe	Thr	Trp	Cys	Leu	Glu	Ile	Arg	Ala	Ile	Pro	Lys	Lys	Ala	Phe	Leu
	370					375					380				
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385				390					395						400
Gln	Glu	Leu	Cys	Ser	Lys	Gln	Gly	Ala	Ala	Asp	Tyr	Ser	Arg	Phe	Val
			405					410					415		
Arg	Asp	Ala	Cys	Ala	Cys	Leu	Leu	Asp	Leu	Leu	Leu	Ala	Phe	Pro	Ser
		420						425					430		



Cys Gln Pro Pro Leu Ser Leu Leu Leu Glu His Leu Pro Lys Leu Gln  
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 Pro Arg Pro Tyr Ser Cys Ala Ser Ser Ser Leu Phe His Pro Gly Lys  
 450 455 460  
 Leu His Phe Val Phe Asn Ile Val Glu Phe Leu Ser Thr Ala Thr Thr  
 465 470 475 480  
 Glu Val Leu Arg Lys Gly Val Cys Thr Gly Trp Leu Ala Leu Leu Val  
 485 490 495  
 Ala Ser Val Leu Gln Pro Asn Ile His Ala Ser His Glu Asp Ser Gly  
 500 505 510  
 Lys Ala Leu Ala Pro Lys Ile Ser Ile Ser Pro Arg Thr Thr Asn Ser  
 515 520 525  
 Phe His Leu Pro Asp Asp Pro Ser Ile Pro Ile Ile Met Val Gly Pro  
 530 535 540  
 Gly Thr Gly Ile Ala Pro Phe Ile Gly Phe Leu Gln His Arg Asn Ser  
 545 550 555 560  
 Lys Asn Asn Thr Gln Met Glu Ile Leu Glu Gln Cys Gly Cys Phe Leu  
 565 570 575  
 Ala Ala Gly Ile Arg Ile Gly Ile Ile Tyr Ser Glu Lys Ser Ser Asp  
 580 585 590  
 Ile Ser Leu Ser Met Gly Ser Leu Ile Arg Phe Pro Ser Gln Glu Met  
 595 600 605  
 Leu Leu Leu Gly Arg Arg Lys Pro Gln Gln Ser Met Tyr Lys Thr Thr  
 610 615 620  
 Ser Ser Phe Met Ala Ser Arg Trp Arg Glu Ser Ser Ser Arg Arg Thr  
 625 630 635 640  
 Ala Ile Phe Met Cys Val Glu Met Gln Arg Ile Trp Pro Arg Met Tyr  
 645 650 655  
 Met Met Pro Leu Cys Lys Ala Lys Arg Leu Glu Leu Lys Asn Lys Gln  
 660 665 670  
 Lys Pro Trp Pro Leu Lys Lys Lys Asn Ala Thr Phe Arg Ile Phe Gly  
 675 680 685  
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<210> 49  
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 <212> DNA  
 <213> Homo sapiens

<400> 49  
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23

<210> 50  
 <211> 26  
 <212> DNA  
 <213> Homo sapiens

<400> 50  
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26

<210> 51  
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 <212> DNA  
 <213> Homo sapiens

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tttgaccgga tggcagcagg tggccccctc tacatagacg tgacctggca cccagcaggt 300
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ccaatagggt accagtggga agaggaggag ggaggcttca actacgcagt ggacctgggtg 540
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gtgaaggcat gcaccgacat gggcatcact tgccccatcg tccccgggat ctttcccatc 780
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<210> 52
<211> 20
<212> PRT
<213> Homo sapiens

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<400> 52
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<210> 53
<211> 23
<212> PRT
<213> Homo sapiens

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<400> 53

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 Arg Lys Phe Val Lys Glu Ile  
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 <213> Homo sapiens

<400> 54  
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 <212> PRT  
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<210> 56  
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 <212> PRT  
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<400> 56  
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<210> 57  
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<400> 57  
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<210> 58  
 <211> 22  
 <212> PRT  
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<400> 58  
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<210> 59  
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<400> 59  
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<210> 60  
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 Asp Ala Lys Asn Met Ala Lys Asp Val  
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<210> 61  
 <211> 26  
 <212> DNA  
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<400> 61  
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<210> 62  
 <211> 27  
 <212> DNA  
 <213> Homo sapiens

<400> 62  
 cacttcccaa ccaaaattct tcaaaag 27

<210> 63  
 <211> 9  
 <212> PRT  
 <213> Homo sapiens

<400> 63  
 Lys Arg Tyr Leu Gln Asp Ile Trp Ser  
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